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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/362,598	07/28/1999	JOEL V. WEINSTOCK	3948/79934	7062
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PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			EXAMINER	
			ZEMAN, ROBERT A	
		ART UNIT	PAPER NUMBER	
		1645		

DATE MAILED: 11/14/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/362,598	WEINSTOCK ET AL.
	Examiner Robert A. Zeman	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 07 September 2001.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 24,26 and 28-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 24,26 and 28-32 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) Other: _____

DETAILED ACTION

The amendments and responses filed on 7-30-2001 and 9-7-2001 are acknowledged.

Claims 24, 26 and 28-32 are pending and currently under examination.

The examiner acknowledges Applicant's statement concerning the sequence listing.

While there is a copy of the notice to comply in the file, apparently Applicant's copy was not sent unbeknownst to the examiner.

Objections Withdrawn

The objection to the specification is withdrawn in light of the amendment thereto.

Claim Rejections Withdrawn

The rejection of claims 24, 26 and 28-32 rejected under 35 U.S.C. 103(a) as being unpatentable over Metwali et al. (Journal of Immunology, Vol. 157, pages 4546-4553, 1996) in view of Boros et al. (Journal of Exp. Medicine, Vol. 132, pages 488-507, 1970) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 24, 26 and 28-32 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method of determining the immune response the co-infection of mice with *M. avium* and *S. mansoni* (either with or without TNBS treatment) or the infection of mice with *T. muris* (with TNBS treatment) by determining the amounts of IL-4 and IFN- γ , does not reasonably provide enablement for a method of screening an helminthic parasite preparation for one or more components that reduce excessive Th1 immune responses, wherein said preparation is prepared by fractionating and sub-fractionating the helminthic preparation is maintained for reasons of record. The specification still does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues:

1. Applicant provides detailed teachings (pages 20-31) on how to obtain fractions and sub-fractions of helminthic homogenates.
2. The Examiner acknowledges that said homogenization methods are routine in the art.
3. Applicant provides detailed teachings in the specification of assays to evaluate which fractions and sub-fractions of an helminthic homogenate possess the requisite biological activity of reducing an excessive Th1 response both *in vitro* (pages 24-39) and *in vivo* (pages 21-22 and 31).
4. Applicant does not understand the Examiner's requirement that Applicant describe the molecular weights of components obtained from fractions and sub-fractions and to identify which sub-fractions would possess the claimed functions since the end result of the claimed

method is to identify components of helminthic homogenates which reduce an excessive Th1 responses.

5. In the method described on page 38, the mycobacterial antigens were not necessary to reduce an excessive Th1 response but were used to enhance a Th1 response in order to create a useful model.

6. It is unclear how methods of identifying fractions and sub-fractions with a particular biological activity are routine in the art under 35 U.S.C. 103(a) yet not be enabled under 35 U.S.C. 112, first paragraph.

Applicant's arguments have been fully considered and deemed non-persuasive. Applicant is reminded that the aforementioned rejection is a scope of enablement rejection. As outlined previously the specification provides no guidance with regard to how **one would obtain sub-fractions of the homogenate** and which sub-fractions would possess the claimed functions. The specification does not disclose how the **sub-fractions** were obtained and used in the assay. Additionally, the specification provides no showing of fractionation or a sub-fractionation of helminthic preparations.

The specification is equally silent on how one would perform the "assay" step of the claimed methods *in vivo*. The specification provides no guidance on what parameters or markers are measured, how said parameters or markers are measured or even how samples are obtained. Given the total lack of guidance provided by the specification showing sub-fractionation of preparations and how one would perform the claimed method *in vivo*, it would require undue

experimentation by one of skill in the art to make and use the invention commensurate in scope with the claimed subject matter.

With regard to Point 1: pages 20-31 of the specification do not disclose detailed teachings on how to obtain fractions and sub-fractions of helminthic homogenates. Said passages disclose prophetic helminthic parasite compounds (pages 20-21), flow cytometry techniques (page 22), ELISAs (pages 23-24), ELISPOT assays (page 24) and broad methodologies for the evaluation of various disease states including: inflammatory bowel disease; Rheumatoid arthritis; Lupus; Juvenile Insulin-dependent Diabetes Mellitus ; Sarcoidosis; Multiple Sclerosis; Autoimmune thyroiditis; Colon polyps/cancer; and allergic airway diseases. Said passages do not disclose any methodology steps for the fractionation or sub-fractionation of helminthic homogenates. Said passages do not even disclose the methodology for acquiring said homogenates.

With regard to Point 2, the Examiner did not acknowledge that said homogenization methods are routine in the art in any of the rejections of record.

With regard to Point 3, said passages, while disclosing broad methodologies for the *in vitro* measurement of components of Th1 and Th2 immune responses, do not disclose on how to obtain fractions and sub-fractions of helminthic homogenates or the utilization of said fractions in the claimed methods. Said passages, contrary to Applicant's assertion, do not disclose the methodologies required to utilize the claimed method *in vivo*. Page 31 merely discloses that *in vivo* models that are useful for assaying helminthic homogenate or fractions exist.

With regard to Point 4, the Examiner is not requiring that Applicant describe the molecular weights of components be obtained from fractions and sub-fractions in order for the claimed invention to be considered enabled.

With regard to Point 5, the mycobacterium antigen, while not required for the reduction of a Th1 response, is an integral component of the method detailed in the working examples.

With regard to Point 6, methods of obtaining and identifying fractions with a particular biological activity are not routine in the art as evidenced by the necessity to cite references disclosing said methods when formulating a rejection under 35 U.S.C. 103(a).

Therefore, for the reasons set forth above the specification is only enabling for an *in vitro* method of determining the immune response the co-infection of mice with *M. avium* and *S. mansoni* (either with or without TNBS treatment) or the infection of mice with *T. muris* (with TNBS treatment) by determining the amounts of IL-4 and IFN- γ .

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 26 and 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Claim 26 is still rendered vague and indefinite by the use of the phrase “one or more further steps of fractionating and assaying. Contrary to Applicant’s argument, said claim is not merely broad but is indefinite. It is unclear what steps would fall under the limitation of “a fractionating and assaying” step. It is equally unclear how one can have one step that both “fractionates” and “assays”. As written it is still impossible to determine the metes and bounds of the claimed invention.

Claim 32 is still vague and indefinite since it is unclear how one would assay activity *in vivo*. Applicant argues that said claim encompasses all assays that are performed *in vivo* to detect a reduction in an excessive TH1 immune response. Applicant's arguments have been fully considered and deemed non-persuasive. Said claim not only fails to identify what, if any, assays would be considered an "*in vivo* assay" to detect a reduction in an excessive TH1 immune response, but fails to recite the active steps required in order to fulfill the stated objective of the method claim.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to a method of screening a helminthic preparation for one or more components that reduce an excessive Th1 immune response. The method comprises preparing and fractionating the preparation and assaying the products for the ability to reduce an excessive Th1 immune response.

The rejection of claims 24, 26 and 28-32 rejected under 35 U.S.C. 103(a) as being unpatentable over Pearce et al. (Journal of Exp. Medicine, Vol.173, pages 159-166, 1991) in view of Pearce et al. (PNAS, Vol. 85, pages 5678-5682, 1988) is maintained for reasons of record.

Applicant argues:

1. Pearce et al. do not actually teach that helminthic preparations of any sort reduce an excessive Th1 response since he merely reports the effect of helminthic preparations on normal Th1 responses.

Applicant's arguments have been fully considered and deemed non-persuasive.

As outlined in the previous Office action, Pearce et al. (1991) disclose a method of identifying antigens from the helminthic parasite *Schistosoma mansoni* for the ability to reduce Th1 responses (see abstract and pages 164-165). Said method comprises preparing parasite antigens e.g. cercariae, soluble extracts of schistosomula, adult worms and eggs (see Material and Methods section, page 160) and screening those preparation for the production of either IFN γ (Th1 response cytokine) or IL-5 (Th2 response cytokine)(see figures 1, 5 and Tables 2-3). The method disclosed by Pearce et al. (1991) differs from the claimed invention in that they do

not explicitly disclose a method of preparing an helminthic parasite antigen comprising homogenizing, separating homogenate fractions and identifying sub-fractions for biological activity. However, Pearce et al. (1988) disclose a method of preparing antigens from *Schistosoma mansoni* that comprises obtaining adult schistosomes, homogenizing in phosphate buffered saline, centrifuging and purifying by immunoaffinity chromatography (see pages 5678-5679). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare schistosoma antigens utilizing the homogenization and immunoaffinity column chromatography disclosed by Pearce et al. (1988) and assay the resulting fractions for the ability to reduce excessive Th1 responses utilizing the assay methods disclosed by Pearce et al. (1991). It would have been expected, barring evidence to the contrary, that the purified schistosoma antigens would be identified for their ability to reduce excessive Th1 responses because Pearce et al. (1991) specifically identify and compare antigens and their abilities to down regulate Th1 cytokine production.

With regard to Applicant's assertion that Pearce et al. do not actually disclose that helminthic preparations of any sort reduce an excessive Th1 response since he merely reports the effect of helminthic preparations on normal Th1 responses: since the components involved in normal and excessive Th1 responses are the same, any assay that measures the reduction of the former is a functional equivalent of the latter. Therefore, it would be obvious to one of skill in the art to utilize a methodology that measures the reduction of a normal Th1 response to measure the reduction of an excessive Th1 response.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Art Unit: 1645

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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LYNETTE R. P. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Robert A. Zeman
November 7, 2002